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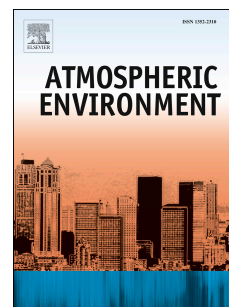
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# Accepted Manuscript

Improving indoor air quality, health and performance within environments where people live, travel, learn and work

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**1 Improving indoor air quality, health and performance within environments**  
**2 where people live, travel, learn and work**

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## 1.0 Introduction

The dramatic episodes of excess mortality arising from the air pollution disasters in the Meuse Valley in 1930<sup>1</sup>, Donora in 1948<sup>2</sup> and London in 1952<sup>3</sup> were pivotal drivers in motivating epidemiological research into this insidious environmental threat. Originating in the UK in the 1950s, such work extended to the United States and Canada and fed into the landmark Harvard Six Cities Study<sup>4</sup> correlating daily incidents of cardiopulmonary mortality with ambient particulate matter (PM). As a result of the subsequent extensive research effort, the associations between short-term and chronic exposure to modern-day outdoor air pollutants (comprising a heterogeneous mix of PM, nitrogen oxides [NO<sub>x</sub>] and ozone [O<sub>3</sub>]) and mortality and morbidity from cardiovascular (CV) and respiratory disease are well documented<sup>5</sup>. Furthermore, emerging epidemiological and experimental data from a growing number of studies suggest a negative influence on a broader number of diseases including adverse birth outcomes<sup>6</sup>, diabetes<sup>7</sup>, neurodevelopment deficits<sup>8</sup> and dementia<sup>9</sup>. Conversely and crucially important, “natural experiments”<sup>10-12</sup>, country-wide changes in air pollution levels<sup>13</sup> and temporary control measures<sup>14</sup> have all provided evidence that reductions in air pollutants can yield observable health benefits – both within a short period of time and over the longer term depending upon the timeframe of the intervention.

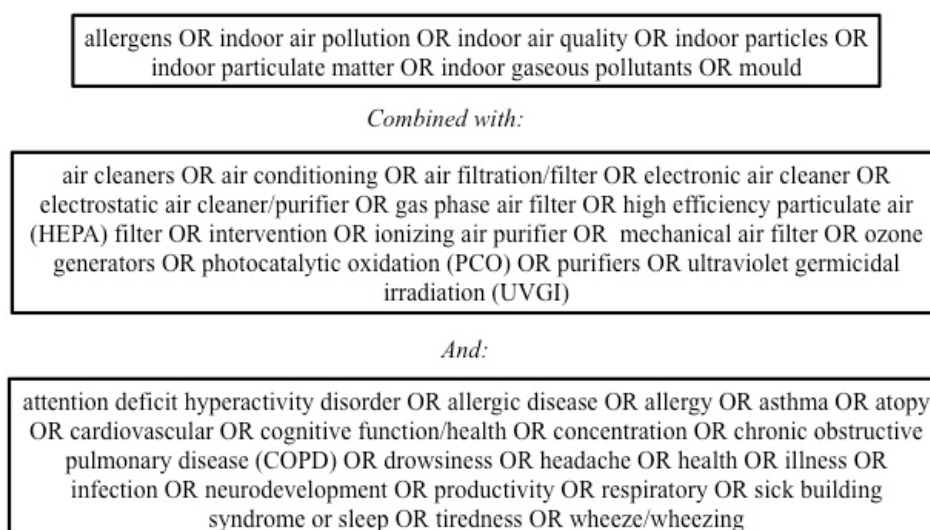
Despite heightened awareness of the associated health risks of air pollution, it is invariably deemed to be solely an outdoor issue, in the general belief that the confines of an inside space, and particularly ones home, offers protection. Owing to marked changes in the lifestyle and working conditions of modern society, particularly in the industrialized nations, individuals spend on average about 90% of their time indoors<sup>15</sup>. It follows therefore that the most important environment in relation to our health and

wellbeing is the indoor environment. Concentrations and sources of indoor air pollutants vary considerably in different parts of the world. In rural homes of developing countries, unvented combustion of solid fuel for household cooking and heating has severe health effects and the greatest impact on mortality<sup>16</sup>. In the megacities of Asia, rapid urbanization and population growth has led to severe indoor air pollution from outdoor sources. These comprise some of the most toxic components of ambient PM, emitted from coal power generation, industry and vehicle exhaust, which dominates a risk to health through an impact on CV disease<sup>17</sup>. In developed countries of the western world, chemicals from cleaning and consumer products, furniture and construction materials, as well as pets and inadequate maintenance of ventilation and air conditioning (AC) systems can deteriorate indoor air quality (IAQ) and lead to a high prevalence of allergies, airway infections and sick building syndrome (SBS)<sup>18-20</sup>.

As a consequence of the increased amount of personal time spent indoors, mounting evidence that exposure to poor IAQ is the cause of excessive morbidity/mortality and confirmation from research into ambient air quality that reductions in air pollutant exposures improve health outcomes, there has been a long standing interest in evaluating the effectiveness of measures to reduce indoor air pollution and improve public health. The objective of this review is to appraise such research on the efficacy of air purification technologies to remove/reduce indoor air pollutants in order to influence health and performance in non-industrial indoor environments where people live, learn, work and travel (homes, schools, offices, cars). Passive purification materials such as paint catalysts are not included. The studies selected for inclusion were collected through searches using PubMed, Embase and Web Science for articles published up until April 2018 (Figure 1). The titles and abstracts of 578 original research and review articles were screened (including studies identified from reference lists of relevant review articles

stemming from the primary search results). Those that were not relevant to the focus of this review were discarded, leaving 483 articles that were then appraised in detail. Of these, the studies that have been included in this review are limited to those deemed to be have produced results of special interest, thereby adding to our understanding of how to improve air quality in the most important indoor environments in relation to health, productivity and wellbeing.

**Figure 1: Search terms and strategy**



## 2.0 Indoor air pollution

Owing to a dramatic change in pollution sources, indoor pollutants that we are exposed to today are markedly different and chemically more diverse from those experienced 40 years ago<sup>21</sup>. Older, relatively inert construction materials have been replaced with new, technologically complex products (e.g. polymers, high performance paints). In addition, the development of new building techniques and designs devoted to effective energy saving can result in airtight indoor spaces with inadequate ventilation. The continuous

increase in the number and type of compounds identified indoors is also a consequence of the emergence of more sophisticated and sensitive analytical instruments and an improvement in sampling strategies<sup>21,22</sup>.

## *2.1 Sources of indoor air pollution*

Sources of indoor air pollution can be categorized into endogenous contamination, reaction products within the indoor environment and penetration of outdoor pollutants. Endogenous pollutants constitute emissions from building and DIY materials, cleaning and personal products, cooking, environmental tobacco smoke (ETS), human metabolism and other biological sources such as mold, pets and house dust mites. The direct emission of primary pollutants from indoor sources is complicated by a wealth of predominantly uncharacterized indoor chemical transformations through which ambient pollutants can be degraded<sup>23</sup> and secondary pollutants can be formed from indoor gas-phase reactions<sup>24</sup>. Recent findings of indoor multi-phase chemistry include diffuse oxidation with possible reactive radical production when using chlorine bleach to wash work surfaces<sup>25</sup> and the oxidative ability of human occupancy to reduce O<sub>3</sub> concentrations<sup>26</sup> and at the same time rapidly increase carbonyl compounds<sup>27</sup>. Pollutants of particular concern that infiltrate from outdoors include PM, and nitrogen dioxide (NO<sub>2</sub>) produced from industry, road traffic, power stations as a consequence of the combustion of fossil fuels, and O<sub>3</sub> generated at ground level by atmospheric reactions of UV light with NO<sub>x</sub> and hydrocarbons.

## *2.2 Factors governing indoor air quality*

Factors governing pollutant concentrations, exposures and public health consequences in occupied indoor environments are complex in number and diversity. In simple terms they are categorized as follows: (a) attributes of the pollutants including their chemical

structure, dynamic properties (e.g. reactivity of gases, size of particulates) and outdoor air concentration that in turn are influenced by ambient environmental conditions (e.g. temperature, wind speed/direction); (b) the design, construction and state of repair of the building such as the types and condition of materials that comprise surfaces, floors and furnishings, the air-exchange rate (ventilation) and presence/effectiveness of air cleaning processes; (c) the timing of presence within the indoor space, occupant density, lifestyle, habits and behaviors. The three widely recommended basic strategies to enhance IAQ are source control to avoid indoor and outdoor emissions, provision of adequate ventilation and air cleaning technologies to achieve further improvements when warranted. Whilst reducing the pollution source is the universally preferred approach, often this is not possible and ventilation increasingly presents challenges in terms of building energy use and because clean outdoor air is far from a given in many areas around the world. The use of air cleaners that do not involve the energy costs of moving and conditioning outdoor air are therefore receiving increasing attention as a strategy to remove unwanted particles and gases.

### *2.3 What is acceptable indoor air quality?*

In 2010, the World health Organization (WHO) issued guidelines on protecting the public from health risks associated with exposure to chemicals commonly present in indoor spaces<sup>28,29</sup>. Other organizations have also adopted guidelines such as the US Environmental Protection Agency's (EPA) voluntary IAQ guidance for multifamily building upgrades<sup>30</sup> and schools<sup>31</sup>. In England, guidance on IAQ at home is currently under consultation and development<sup>32</sup>. Regulatory controls on indoor air pollution are limited to ventilation standards of building regulations that are widely believed to be inadequate in relation to health<sup>33</sup>. They are designed to meet acceptable air quality and



comfort requirements, specified by a percentage that does not express dissatisfaction with IAQ and/or the intensity of odor. This is a subjective response that results in a measure of perceived air quality. Whilst comfort is an important parameter, some argue that it does not fully reflect serious health impacts (e.g. asthma, allergies, COPD, CV diseases) that are associated with exposures to pollutants present in indoor air<sup>34</sup>. Indeed, the link between comfort and health is not clearly established and it is not certain whether ensuring comfort requirements will abate health risks and vice versa. On the other hand and as discussed by Ole Fanger<sup>35</sup>, “the perceived air quality ... may in many cases also provide a first indication of a possible health risk”. Defining an IAQ target is further complicated by limited data on the relationship between the multitude of indoor pollutants (as well as reaction products and transformations) and health<sup>29</sup>, large differences among individuals’ susceptibility and preferences and the challenge of ensuring energy performance goals are met without jeopardizing the quality of our indoor environment, life and health. Whilst data is limited on measured ventilation rates in European countries<sup>36</sup>, a review of domestic ventilation in 12 European countries concluded that an air exchange rate (air changes per hour) of  $0.5\text{h}^{-1}$  - the minimum requirement in many European standards - might not satisfy health criteria<sup>37</sup>.

### 3.0 Air cleaners

An air purification plant may be a component of the ventilation and AC system that addresses multiple spaces in a building, or a stand-alone, portable or fixed (wall, window or ceiling mounted) device that purifies a room or a portion thereof. Factors to be taken into consideration in selecting the most effective air cleaning system include the target pollutant phase, long-term performance, energy consumption and the formation of unwanted by-products. Air purification technologies are briefly described below. For more detailed information on working principles, target pollutants, performance and

problems that may occur during their application, the reader is directed to several comprehensive reviews that have been published in recent years<sup>38-42</sup>.

### *3.1 Mechanical ventilation*

Mechanical filtration is a simple and extensively utilized technique to substantially capture and retain particulate air pollutants<sup>43</sup>. Performance depends on the type of filter (flat, pleated, HEPA), filter media material and coatings, airflow through the system, size of particle contaminant and filter age<sup>43,44</sup>. The most commonly used HEPA filters are over 95% efficient in removing particles of all sizes<sup>45</sup>. Owing to particle saturation and associated pressure loss, filters must be replaced to maintain removal efficiency, guard against sensory pollution and new sources of contamination in the form of harmful microorganisms<sup>46</sup>.

### *3.2 Electronic air filtration*

Electronic air filtration systems fall into 2 types. Electrostatic precipitators (ESP) are medium cost devices, generating ions that attach to and electrically charge particulate pollutants as they pass through the device. Once charged, the particles are deflected by an electric field onto on a series of positive and negative charged cleanable plates. The second type constitutes high cost air ionizers or ion generators that disperse positive and negative ions into the atmosphere that attach airborne particles. In that these devices do not possess collector plates, the charged particles attach to nearby surfaces or to one another forming heavier particles that promote deposition. Electronic air filtration is efficient at removing particles (90% and 95% for 0.3 - 6  $\mu\text{m}$  particles for electrostatic filters and ion generators respectively) and results in slower pressure loss than mechanical filters, however a high relative humidity can negatively affect removal efficiency, plus they can generate hazardous charged particles and unwanted oxidation

188 by-products<sup>47,48</sup>

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### 190 3.3 Adsorption

191 Adsorption is a high performance technique (> 90% removal efficiency) that removes  
192 gaseous pollutants (VOCs, O<sub>3</sub>, NO<sub>2</sub>, SO<sub>2</sub> and hydrogen sulfide)<sup>49,50</sup> using an appropriate  
193 adsorbent, such as activated carbon and hydrophobic zeolites<sup>51,52</sup>. Disadvantages include  
194 a compromised efficiency at a high relative humidity<sup>50</sup>, the need to regularly replace the  
195 adsorbents to prevent waste pollutants re-entering the atmosphere and the potential of  
196 airborne bacteria to thrive on carbon sorbents<sup>53</sup>.

### 197 3.4 Ozone generators

198 Ozone generators use UV radiation or a corona discharge to produce O<sub>3</sub> from oxygen to  
199 eliminate microbial agents and odours<sup>54</sup>. However, O<sub>3</sub> concentrations that do not exceed  
200 typical exposure limits (50-100 ppb) cannot guarantee efficient removal of indoor air  
201 contaminants<sup>49,54</sup>, and moreover reactions with terpenes can produce potentially harmful  
202 secondary organic aerosol, carbonyls, carboxylic acids and free radicals<sup>55</sup>. For these  
203 reasons, O<sub>3</sub> generators are not recommended by public health agencies as a safe and  
204 effective way to control indoor air pollutants<sup>56</sup>.

### 205 3.5 Ultraviolet germicidal irradiation

206 Ultraviolet germicidal irradiation (GI) uses UV radiation from photoreactor lamps to  
207 destroy bioaerosols such as airborne viruses, bacteria, dust mites, animal dander and  
208 mould (or such contaminants growing on HVAC surfaces) through photolysis oxidation  
209 or UV photolysis<sup>57</sup>. It can be configured within HVAC surfaces or independently as a

unit installed on the wall or suspended from ceilings thereby disinfecting infectious bioaerosols in upper environments, while maintaining occupant safety below. A limited application is a consequence of a propensity to produce  $O_3$  and radicals<sup>38</sup>.

### 3.6 Photocatalytic oxidation

Photocatalytic oxidation (PCO) promotes, at ambient temperatures, the destruction of many organic compounds in a stepwise reaction into water and  $CO_2$  using UV light and a semiconductor as the nano-catalyst<sup>41,58-60</sup>. Devices employing this technique are cost effective, require little maintenance<sup>61</sup> and can be incorporated into new and existing HVAC systems<sup>58</sup>. Reaction rates are influenced by many factors including the pollutant type and concentration, relative humidity, air-flow rate, residence time, UV radiation wavelength and intensity and a number of catalyst features<sup>58,59</sup>. Drawbacks that currently prevent widespread commercial application include moderate performance and short lifetime of the catalyst. Furthermore, the process can generate intermediates and by-products that (a) are toxic to human health and (b) can deactivate the active sites of the catalyst<sup>62</sup>. As an example, 20 VOCs reaction intermediates have been identified when investigating the PCO of limonene (750 ppbv; dry air conditions) – the naturally occurring hydrocarbon used to infuse lemon scent into household cleaners and fragrances<sup>63</sup>.

### 3.7 Cold plasma or cold thermal plasma

Cold plasma or non-thermal plasma based cleaning techniques utilize a high voltage electrical discharge to eliminate PM and biological pollution through precipitation and oxidation<sup>39</sup>. In addition, the production of free radicals and oxidant species transform VOCs into  $CO_2$  and water<sup>64</sup>. Efficiencies in eliminating bacterial and fungal species of over 95% and 85-98% have been reported<sup>65</sup>. Since electron density and that of reactive

radicals are modified by water vapor, efficacy of decomposition can be either enhanced or suppressed, depending on the pollutant and the dominant pathway of destruction. For example, increasing relative humidity has been shown to enhance removal of toluene, n-butane and formaldehyde, this negatively affects the degradation of tetrachloromethane, methanol and dimethyl sulfide<sup>66,67</sup>. Drawbacks that currently preclude the application of this technology into commercial devices include poor energy efficiency<sup>68</sup> as well as the formation of O<sub>3</sub>, NO<sub>x</sub>, and other hazardous organic by-products<sup>69,70</sup>.

### *3.8 Air cleaner performance*

The single-pass removal efficiency (generally within a 0-100% range) is the most commonly used performance metric to describe an air cleaner and is defined as the fraction of the pollutant entering an air cleaner that is subsequently removed by the cleaner<sup>71</sup>. For particulate pollutants, removal is a strong function of particle size - lowest for particles with aerodynamic diameters of 0.2– 0.3  $\mu\text{m}$  and higher for both larger and smaller ones<sup>72</sup>. Removal efficiency will also vary according to rate and duration of airflow through the device, filtration media loading<sup>72,73</sup>, fouling of corona wires<sup>74</sup>, UV lights<sup>75</sup> and activated carbon<sup>76</sup> and the way in which the air cleaner is installed and maintained<sup>77</sup>. A more relevant performance parameter when comparing air cleaning devices is therefore the product of single-pass removal efficiency and the airflow rate through the cleaning device. This is termed the clean air delivery rate (CADR) and is equivalent to the volume of clean air provided to the space by an air cleaner. There are several standard laboratory test methods to measure efficiency of particle filtration (ASHRAE 52 [minimum efficiency reporting value – MERV 1-16] and European EN 779 [G1 – F9]) and gas cleaning devices (ASHRAE 145.2 and ISO 10121-2). It should be borne in mind that these tests, conducted in controlled environments over a few minutes

or hours, may not directly reflect the effectiveness in a real living conditions characterized by time- and space-varying indoor emissions, outdoor infiltration of particles, ventilation, and airflow patterns.

## **5.0 Effects of air cleaners on health outcomes in homes**

Reviews of intervention studies using standalone air purifiers and conducted amongst free-living participants residing in their own homes to evaluate the potential health benefits began with a report by the Institute of Medicine<sup>78</sup>. Others followed<sup>79-82</sup>, including a meta-analysis by McDonald et al<sup>83</sup>, all generally assessing a subset of the same studies appraised by the IOM. On the whole, the evaluated studies were deemed to have weak designs and the reviews generally conclude that filtration devices led to only small improvements in allergy and asthma outcomes. The meta-analysis indicated that particle filtration was associated with statistically significant improvements in total symptoms (5-8%) and sleep disturbance (10%). The review by Fisk<sup>84</sup> included previously reviewed studies, plus 16 additional intervention studies (published from 2003 to 2012) that featured much stronger designs. This review of the literature concluded that:

- particle filtration can modestly (7–25%) reduce allergy and asthma outcomes, especially in homes with pets;
- more consistent improvements in health may be achieved by delivering filtered air to the breathing zone of sleeping individuals with asthma/allergic diseases;
- although limited evidence indicates that particle filtration is not very effective in reducing acute health outcomes outside of asthma and allergy, statistically significant improvements in microvascular function (MVF), a marker that predict future adverse coronary events, have been cited;

- modeling studies suggest that the largest potential benefits of particle filtration may be reductions in morbidity and mortality as a consequence of lessening indoor exposures to particles from outdoor air.

Studies published from 2013, investigating the health benefits of air cleaners in homes (a) characterized by unremarkable ambient air pollution (Table 1), (b) impacted by wood smoke (Table 2) and (c) within industrial cities of developing countries with particularly poor outdoor air quality (Table 3) are discussed below.

### *5.1 Homes characterized by relatively low baseline air pollution (Table 1)*

Three studies conducted in urban areas close to major roads all adopted randomized, double-blinded crossover interventions in which older adults were exposed to consecutive periods of filtered and non-filtered air by HEPA filters built into AC units<sup>85-87</sup>. Despite reductions in particle number concentrations ranging from 30 to 75%, no improvement in health outcomes - primarily markers of CV disease risk - were observed. In fact Padró-Martínez et al reported significantly higher interleukin-6 (IL-6) concentrations after a 21-day HEPA filtration<sup>86</sup>. Another study by the same researchers found no benefit in terms of reduced inflammation among adults in homes receiving HEPA filtration despite reducing PNC by 50-85% and findings were not appreciably altered upon pooling the 2 datasets<sup>87</sup>. Factors that may explain the inability to detect improvements in health outcome measures include relatively low baseline pollution concentrations and small exposure gradients, carry-over effects in the absence of washout periods and questionable compliance in keeping windows shut and/or HEPA devices running at all times. In fact Karottki et al<sup>85</sup> did report highly variable filtration efficacy in both the living rooms and bedrooms where the true/sham interventions took place. Exposure misclassification (owing to lack of time-activity information), uncontrolled confounding and unsuccessful

randomization (with respect to baseline IL-6 concentrations and use of anti-inflammatory drugs) are additional factors that may have contributed to the general lack of health benefit as well as the unexpected negative IL-6 association<sup>86</sup>. That is to say, the effects of changes in PM concentrations on CV disease markers might be masked by medication per se or more difficult to detect because of the existing disease they are taken for. In contrast to the earlier tranche of air purifier intervention studies, very few recent investigations have focused on respiratory outcomes. One exception demonstrated that the introduction of portable HEPA air purifiers into living rooms and bedrooms were effective in significantly reducing indoor PM<sub>2.5</sub> concentrations and nasal symptom scores in asthmatic children<sup>88</sup>. A trend towards an improvement in childhood asthma control test scores and mean evening peak flow rates was also reported. Investigations focusing on the effectiveness of air purifiers to remove secondhand smoke (SHS) has begun with a pilot study deploying HEPA air purifiers in conjunction with SHS education into the homes of nonsmoking pregnant women or post-partum mothers (any smoking status) with infants (0-12 months)<sup>89</sup>. The homes had at least one smoker and the study reported significantly decreased indoor PM<sub>2.5</sub> concentrations and salivary cotinine levels in non-smoking women (but not infants) but no change in air nicotine concentrations. The latter is consistent with previous studies addressing SHS<sup>90,91</sup> and may be attributed to the inability of carbon filters to remove many of the carcinogenic gas phase pollutants from tobacco smoke<sup>44</sup>.

A number of modeling studies have evaluated scenarios of improved home filtration by integrating mass balance models, epidemiological functions and monetary valuations to estimate health and economic impacts of reducing mortality associated with indoor particle concentrations<sup>92-94</sup>. Zhao et al<sup>92</sup> projected that the use of filters (MERV 5 to



HEPA) in HVAC systems of homes in 22 US cities would reduce premature mortality by 0.002–2.5% and increase life expectancy by 0.02–1.6 months, equating to annual economic benefits ranging from \$1 to \$1348 per person. Another study modeled the reductions in mortality in Toronto from replacing standard furnace filters with MERV 15 rated filters in homes constructed to the latest energy efficiency standards (R2000). Use of mechanical HVAC systems, improved filtration and tighter building envelopes were identified as the key factors influencing predicted PM<sub>2.5</sub> exposure reductions (29% in summer and 28% in winter) and a 26% reduction in non-accidental mortality. The citywide residential retrofitting was predicted to save US\$2.3 billion/year in health care costs. In modeling scenarios adopted by Fisk & Chen<sup>94</sup>, the largest predicted mortality reductions, at approximately 2 per year per 10 000 population, resulted from interventions with continuously operating PAC with HEPA filters in homes. Economic benefits always exceeded costs (in most cases by more than a factor of 10), whilst larger increases in the mortality reductions per unit population and the benefit-to-cost ratios were achieved by restricting interventions to homes of older people. A model has also been developed to evaluate potential benefits of O<sub>3</sub> control by in-duct AC filtration in homes in 12 US cities in 5 different climate zones<sup>95</sup>. Average indoor O<sub>3</sub> removal effectiveness ranged from 4 to 20% and the mean predicted benefit/cost ratios were for >1.0 in 10 of the 12 cities. That benefits of residential AC filtration were greatest in homes with high HVAC use located in cities with high seasonal O<sub>3</sub> suggests an important contribution from secondary atmospheric chemistry in eliciting health effects within the studied localities.

358 **Table 1. Summary of studies investigating health effects of air filtration in homes characterised by relatively low baseline air pollution**

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Study	Study design, purifier type, filtration site, intervention duration	Exposure focus, health outcomes, location, study population	Indoor pollutant reduction & health outcome	Author conclusion
Karottki et al 2013	Double-blind, crossover randomized to true/sham filtration  HEPA filter in AC units  Living room & bedroom  2 x 14 d; no washout	UFP, PM <sub>2.5</sub> , UVPM, BC, PAH  MVF, lung function (FEV <sub>1</sub> /FVC), BP, inflammation (CRP, WBC), markers of lung cell & monocyte surface damage  Greater Copenhagen, Denmark 48 non-smoking elderly adults; mean age 67 years	PM <sub>2.5</sub> 46% (4.3 µg/m <sup>3</sup> with filtration & 8.0 µg/m <sup>3</sup> without filtration) in living room, 51% (3.7 µg/m <sup>3</sup> with filtration & 7.6 µg/m <sup>3</sup> without filtration) in bedroom; PNC 30%; UVPM 44%; BC 54%; PAH: 48%  ↔ MVF, BP, lung function, biomarkers	No improvement in MVF or lung function or detectable reduction in systemic inflammation, monocyte activation or lung cell damage in this elderly population, including people taking vasoactive medication, but with relatively low initial exposure levels.
Padro-Martinez et al 2015	Double-blind, crossover randomized to true/sham filtration  Window mounted HEPA  Living room  2 x 21 d; no washout	UFP  Inflammation (IL-6, CRP, TNF-RII), coagulation (fibrinogen), BP  Somerville, Massachusetts, USA 20 adults; mean age 53 years	PNC: 21-68% ↑IL-6 (49.6%) ↔ CRP, fibrinogen, TNF-RII, BP	There is a need for more effective filtration to reduce UFP & to increase sample sizes to see biological effects.
Brugge et al 2017	Double-blind, crossover randomized to true/sham filtration  Window mounted HEPA  Living room or bedroom  2 x 21 d; no washout	UFP  Inflammation (IL-6, CRP, TNF-RII)  Boston & Chelsea, Massachusetts, USA 24 adults; mean age 64 years	PNC: 75%  ↔ Inflammation	No benefits were found on blood biomarkers for CVD risk, however valuable lessons were learned that could inform future trials.
Park et al 2017	Randomized to no or 2 air purifiers  Portable HEPA  Living room & bedroom  12 weeks	PM <sub>2.5</sub>  cACT, peak flow rate, nasal symptoms (congestion, rhinorrhea, nasal itching, sneezing)  Fresno, California, USA 17 children with asthma/allergic rhinitis (control group n = 8, mean age 14 years; active group n = 9, mean age 10 years)	PM <sub>2.5</sub> 43% (4.3 µg/m <sup>3</sup> with filtration & 7.4 µg/m <sup>3</sup> without filtration)  ↓total (27%) & daytime (30%) nasal symptoms ↔ cACT, peak flow rate	Indoor PM <sub>2.5</sub> levels can be reduced in homes by using air purifiers with HEPA filters & these improvements in indoor air quality can improve nasal symptoms scores.
Rice et al 2018	Pilot single arm study to evaluate feasibility of deploying 2 PACs in the homes of pregnant women & children	PM <sub>2.5</sub> , air nicotine  Salivary cotinine	↓ 45% PM <sub>2.5</sub> (17 µg/m <sup>3</sup> with filtration & 31 µg/m <sup>3</sup> without filtration) ↔ Air nicotine	Air purifiers with SHS education is a feasible intervention in homes of women & infants, achieving reductions in indoor PM <sub>2.5</sub> & salivary cotinine in

	Portable HEPA & SHS education  Living area & adult/child bedroom  28 days	Baltimore, USA 50 women; mean age 27 years (pregnant non smokers n = 18; or post-partum any smoking status n = 32) with an infant age 0–12 months	↓ 35% non smoking women salivary cotinine ↔ Child salivary cotinine	non-smoking adults.
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↔; no statistically significant change; ↓ or ↑ statistically different change

BC: black carbon; BP: blood pressure; cACT: childhood asthma control test; CRP: C-reactive protein; FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; HEPA: high efficiency particle arresting; IL-6: interleukin-6; MVF: microvascular function; PAH: polycyclic aromatic hydrocarbon; PM<sub>2.5</sub>: particulate matter < 2.5 µm in diameter; PNC: particle number count; TNF-RII: tumor necrosis factor receptor type II; UFP: ultrafine particle; UVPM: UV absorbing PM; WBC: white blood cell count

## 5.2 Homes afflicted by landscape or residential wood smoke

The use of air cleaners in homes of smoke impacted communities to either reduce exposure<sup>96-101</sup> or mitigate health effects<sup>102-104</sup> has and continues to attract interest. Regional-scale smoke pollution stems from wildfires, large-scale biomass burning to clear land for agriculture and in/outdoor residential wood burning and is associated with mortality and cardiorespiratory morbidity<sup>105</sup>, declines in lung function/respiratory symptoms in children and hospital visits<sup>106,107</sup>. The research into effectiveness of PACs in smoke impacted communities is particularly relevant since to mitigate exposures to smoke during prescribed burns and wildfires, a common public health recommendation includes remaining indoors with doors and windows shut. An earlier study by Allen et al<sup>102</sup> already reviewed by Fisk et al<sup>84</sup>, reporting a 9.4% increase in endothelial function and 33% decrease in the C-reactive protein (CRP) in healthy adults following one-week filtration in wood burning homes, has been included in this discussion to add context to the more recent investigations (Table 2). Despite using a very similar randomized crossover study design and population in wood smoke-impacted community, and reporting significant reductions in PM<sub>2.5</sub> and the wood smoke marker levoglucosan, the same group of workers subsequently found no relationship between PM<sub>2.5</sub> exposure and endothelial function or markers of inflammation and oxidative stress<sup>103</sup>. This may be explained by lack of woodstove use among participants and lower outdoor levoglucosan concentrations in the latter (13-20 ng/m<sup>3</sup>) versus the earlier (530-613 ng/m<sup>3</sup>) study. In addition, compliance in operating the air cleaners at the highest comfortable speed may have been a factor since indoor PM<sub>2.5</sub> concentrations did not decrease in seven of 44 homes during the week with HEPA filters in place. In rural areas of Montana, Idaho, and Alaska, where residential wood combustion is a major source of ambient and indoor PM<sub>2.5</sub> and the primarily means of heating, the impact of either improved technology

wood burning stoves or portable electret filtering devices (over one winter period) in improving health measures in asthmatic children has been investigated<sup>104</sup>. Whilst neither intervention improved the subjective pediatric asthma quality-of-life measures, the air-filtration device brought about a 11.8% improvement diurnal peak flow variability (a measure of airway hyperactivity). Fisk et al<sup>108</sup> have modeled potential health benefits and costs associated with 6 air filtration interventions in homes during a 10-day wildfire smoke event that substantially elevated particle concentrations and hence smoke exposure in a six-county region in southern California in 2003. Three out of six intervention scenarios involved the use of PACs as (a) a stand-alone intervention or (b) in conjunction with low or (c) high efficiency in duct filtration and brought out reductions in indoor PM<sub>2.5</sub> concentrations by 45, 51 and 62% respectively. Results estimated that targeted PAC use alone would have reduced smoke-related deaths and hospital admissions in the general population by 30 and 45% respectively and in the elderly by 50 and 78% respectively. Mortality-related economic benefits for interventions incorporating PAC use exceeded intervention expenditure and this cost effectiveness (intervention costs: US\$368 million; health-related benefits: US\$445 million) increased by intervening in the homes of older people.

**Table 2. Summary of studies investigating health effects of air filtration in homes of woodsmoke impacted communities**

Study	Study design, purifier type, filtration site, intervention duration	Exposure focus, health outcomes, location, study population	Indoor pollutant reduction & health outcome	Author conclusion
Allen et al 2011	Single-blind, crossover randomized to true/sham filtration  Portable HEPA  Main activity room & bedroom  2 x 7 d; no washout	PM <sub>2.5</sub> , levoglucosan (wood smoke marker)  Endothelial function, inflammation (CRP, IL-6; band cells), oxidative stress (MDA, 8-iso-PGF <sub>2</sub> α)  Smithers, British Columbia, Canada  45 healthy adults; mean age 43 years	PM <sub>2.5</sub> : 59% (4.6 µg/m <sup>3</sup> with filtration & 11.2 µg/m <sup>3</sup> without filtration); levoglucosan: 74% (33 ng/m <sup>3</sup> with filtration & 127 ng/m <sup>3</sup> without filtration)  ↑endothelial function (9.4%); ↓CRP (33%) ↔ IL-6; oxidative stress markers	Predictors of cardiovascular morbidity, can be favourably influenced by reducing indoor particle concentrations.
Kajbafzadeh et al 2015	Single-blind, crossover randomized to true/sham filtration  Portable HEPA  Living room & bedroom  2 x 7 d; no washout	PM <sub>2.5</sub> , levoglucosan  Endothelial function, inflammation (CRP, IL-6, band cells)  Vancouver, British Columbia, Canada  20 healthy adults; mean age 51 years	PM <sub>2.5</sub> : 48% (3.4 µg/m <sup>3</sup> with filtration & 6.5 µg/m <sup>3</sup> without); 60% LG (11.8 ng/m <sup>3</sup> during filtration & 29.3 ng/m <sup>3</sup> during control periods)  ↔ endothelial function, CRP, IL-6, band cells	No evidence of an association between cardiovascular effects and indoor PM <sub>2.5</sub> among healthy adults in wood smoke-impacted locations.
Noonan et al 2017	Single-blind, crossover randomized to true/sham filtration  Portable electret filter  Living room & bedroom  2 x one winter period; no washout	PM <sub>2.5</sub> , UFP  PAQLQ scores, PEF, dPVF  Montana, Idaho & Alaska, USA in homes impacted by residential wood smoke  92 asthmatic children, mean age 12 years	PM <sub>2.5</sub> : 67%  ↓dPVF (11.8%); ↔ PAQLQ, PEF	Among children with asthma and chronic exposure to wood smoke, an air-filter intervention that improved indoor air quality did not affect quality-of-life measures but was efficacious for improving an indirect measure of airway hyper-responsiveness.

↔; no statistically significant change; ↓ or ↑ statistically different change

CRP: C-reactive protein; dPVF: diurnal peak flow variability; HEPA: high efficiency particle arresting; IL-6: interleukin-6; MDA: malondialdehyde; PAQLQ: Pediatric Asthma Quality of Life Questionnaire; PEF: peak expiry flow; PM<sub>2.5</sub>: particulate matter < 2.5 µm in diameter; UFP: ultrafine particles

### 5.3 Homes afflicted by exceptionally high ambient air pollution

The global public health burden of ambient PM<sub>2.5</sub> is disproportionately felt in developing countries undergoing enormous industrialization and urbanization<sup>109</sup>. Population weighted PM<sub>2.5</sub> exposures average 74.3 and 58.4 µg/m<sup>3</sup> in India and China respectively and together account for >50% of global PM<sub>2.5</sub> mortality<sup>110</sup>. As a consequence of infiltration of outdoor air and emissions from indoor sources such as cooking oil fumes, smoking and human activities<sup>111,112</sup>, indoor PM<sub>2.5</sub> concentrations in Chinese cities can average 80 - 124 µg/m<sup>3</sup><sup>113,114</sup>. Improving outdoor air quality in Asia is proving a gargantuan task, with the risk of any short-term improvements being undone as a result of the ongoing appetite for cheap power and automobile use<sup>115</sup>. Indeed, according to the forecasts of demographic and epidemiological transitions, average PM<sub>2.5</sub> levels would need to decrease approximately 20–30% over the next 15 years to offset the increase in mortality attributable to PM<sub>2.5</sub> levels among aging populations in China<sup>116</sup>. Solving the problem constitutes a long-term goal for generations to come. In the interim, hundreds of millions of individuals will continue to be exposed to hazardous ambient PM<sub>2.5</sub> concentrations far exceeding WHO Air Quality Guidelines. It is not surprising therefore that investigations into the impact of short-term solutions in the form of indoor air filtration devices has been actively investigated (Table 3). Chen et al conducted a double-blind, randomized, crossover study, incorporating a 14 day washout period, among healthy university students living in dormitories in a central urban area of Shanghai<sup>117</sup>. Confining the young adults to their dormitories, equipped with a portable electret filtration device, for 48 hours reduced indoor PM<sub>2.5</sub> concentration, systolic and diastolic blood pressure, a marker of coagulation and some measured metrics of inflammation and platelet activation. Whilst fractional exhaled nitric oxide, an established marker of respiratory inflammation, was reduced, lung function did not change. A subsequent study

of near identical design other than increasing the active/sham intervention to 9 days brought about significant reductions in indoor PM<sub>2.5</sub> concentrations (as well as personal exposure), blood pressure and biomarkers of oxidative stress and inflammation<sup>118</sup>. In contrast to the aforementioned studies, Cui et al<sup>119</sup> examined the cardiorespiratory impact, of a single overnight HEPA air filtration intervention, better approximating the real-world scenario where people only have indoor air filtration for part of the day when they are home. Compared to sham filtration, active purification within student dormitories substantially decreased indoor particle concentrations and significantly improved airway mechanics. No significant improvements in CV function were observed but filtration also lowered von Willebrand factor (26.9%) reflecting reduced risk for thrombosis. Chuang et al<sup>120</sup> investigated whether long-term improvements in IAQ, using electret filtration added to window mounted air conditioners, are beneficial for CV health among adult housewives and househusbands in Taipei. The one-year filtration intervention reduced personal exposure to PM<sub>2.5</sub>, which was associated with improved CV health as evidenced by reduced systolic and diastolic BP and 8-hydroxy-2'-deoxyguanosine, a marker of oxidative stress. An associated reduction in personal VOC exposure was unexpected since the air purifier was not designed to remove gaseous pollutants leading the authors to speculate that aerosolized VOCs could be adsorbed into the filter media. The cardiorespiratory effects of in-home HEPA air filtration for a 2-week period have also been examined in a more susceptible population, namely 23 non-smoking elderly individuals, with and without COPD, residing in Beijing and under instructions to spend much of their time indoors<sup>121</sup>. Following active filtration, significant reductions in indoor PM<sub>2.5</sub> were not associated with detectable improvements in lung function, blood pressure or HRV, suggesting that short-term interventions can be of limited health benefit with exposure to extreme high outdoor air pollution levels. In another susceptible population,



Barn et al<sup>122</sup> investigated the impact of HEPA filter air cleaner use for 5 months during pregnancy on indoor residential PM<sub>2.5</sub> and blood cadmium concentrations (as an indicator of SHS exposure) among non-smoking women in Ulaanbaatar, Mongolia's capital city. Air cleaners lowered indoor PM<sub>2.5</sub> by 29% and blood cadmium by 14% from a geometric mean of 0.23 µg/L to 0.20 µg/L. Whilst these are relatively low concentrations compared with those previously reported for pregnant women, reductions, even from low levels, could have important public health implications. Cadmium is a known carcinogen and in pregnancy has been linked too small for gestational age infants and reduced infant birth weight<sup>123-125</sup>. Air cleaner effectiveness was reduced by 50% after approximately 5 months of use and participants reported using air cleaners for 64% of the study period possibly owing to concerns about noise and electricity.

It is unlikely that every component within the overall ambient PM mix is equally harmful to exposed populations and as a consequence, there has been an enormous drive to identify which components and source are most harmful to health<sup>126</sup>. The mechanisms through which PM elicits ill health are yet to be fully elucidated however current evidence supports an interactive chain of events involving inflammatory responses and oxidative stress<sup>127</sup>. In the light of this, the effectiveness of portable HEPA air cleaners in removing PM<sub>2.5</sub> and its chemical components (organic carbon, elemental carbon, sulfate, nitrate, ammonium, 21 selected metals) and reducing the capacity of particles to elicit damaging oxidative reactions through the generation of reactive oxygen species (ROS) in the indoor environment of 6 Beijing homes has also been assessed<sup>128</sup>. Along with the above mentioned measurements, was an investigation into the relationship between air cleaner use and personal exposure. Whilst the HEPA filter air cleaners substantially lowered indoor PM<sub>2.5</sub> and all its major components, an effect on reducing overall personal exposure was marginal. Since the participant whereabouts was not restricted to

the purified rooms, this was probably the result of activity patterns, bringing about short-time exposures to elevated PM<sub>2.5</sub> concentrations both outdoors (e.g. traffic emissions) and indoors (e.g. cooking emissions) as well as a contribution from the uncharacterized indoor microenvironment. Results of the toxicity assay were indicative of reduced ROS activity in the indoor environment but this did not translate into a reduction in personal exposure to PM-induced ROS. The effects of combined ESP-HEPA filtration on cardiorespiratory disease risk indicators has also been examined by temporarily (during a 39-day intervention) removing either ESPs alone or both ESPs and HEPA filters from 3-part (coarse-ESP-HEPA) air-handling systems<sup>129</sup>. HEPA filter removal increased PM<sub>2.5</sub> concentrations but had no effect on a battery of cardiorespiratory biomarkers. Previous studies evaluating biomarker effects of filtration in healthy adults have shown greater associations after either short (up to 48 hours) or long (after a year) versus after intermediate durations (weeks). Of note, this prompted discussion over the possible presence of a short-term biomarker response, an intermediate-term return to baseline and then a long-term shift in biomarker levels following changes in pollutant exposure lasting days, weeks or a year, respectively. Removal of ESPs decreased O<sub>3</sub> concentrations and this was associated with reductions plasma-soluble P-selectin (marker of thrombosis) and systolic blood pressure, indicating that the concomitant low-level increases in indoor O<sub>3</sub> and O<sub>3</sub>-derived products by this air cleaning technology may impact CV health.

511 **Table 3. Summary of studies investigating health effects of air filtration in homes of Asian megacities**  
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Study	Study design, purifier type, filtration site, intervention duration	Exposure focus, health outcomes, location, study population	Indoor pollutant reduction & health outcome	Author conclusion
Chen et al 2015	Double-blind, crossover randomized to true/sham filtration  Portable electret filter  College dormitory  2 x 48 h; 14 d washout  Participants in dormitory for entirety of intervention	PM <sub>2.5</sub>  Inflammation (CRP, fibrinogen, P-selectin, MCP-1, IL-1 $\beta$ , TNF- $\alpha$ , IL-6, MPO); blood coagulation (sCD40L, PAI-1, t-PA, D-dimer); vasoconstriction (ET-1, ACE); BP; lung function; lung inflammation (FeNO)  Shanghai, China 35 healthy, non-smoking college students; mean 23 years	PM <sub>2.5</sub> : 57% (41.3 $\mu\text{g}/\text{m}^3$ with filtration & 96.2 $\mu\text{g}/\text{m}^3$ without filtration)  ↓MCP-1 (17.5%), IL-1 $\beta$ (68.1%), MPO (32.8%), ↓sCD40L (64.9%); ↓Systolic BP (2.7%), ↓diastolic BP (4.8%); ↓FeNO (17%), ↔CRP, fibrinogen, P-selectin, TNF- $\alpha$ , IL-6, PAI-1, t-PD, D-dimer, vasoconstriction, lung function	Study demonstrated clear cardiopulmonary benefits of indoor air purification among young, healthy adults in a Chinese city with severe ambient particulate air pollution.
Li et al 2017	Double-blind, crossover randomized to true/sham filtration  Portable electret filter  College dormitory  2 x 9 d; 12 d washout  Participants in dormitory much time as possible	PM <sub>2.5</sub>  BP, hormones (CRH, ACTH), insulin resistance, oxidative stress (8-OHdG, MDA, SOD, 8-iso-PGF2 $\alpha$ ) & inflammation (sCD40L, CRP, IL-1 $\beta$ , IL-6, TNF- $\alpha$ , ICAM-1)  Shanghai, China 55 healthy, non-smoking college students; mean 20 years	PM <sub>2.5</sub> : personal exposure: 54% (24.3 $\mu\text{g}/\text{m}^3$ during filtration & 53.1 $\mu\text{g}/\text{m}^3$ during control periods) PM <sub>2.5</sub> : 82% 8.6 $\mu\text{g}/\text{m}^3$ with filtration & 46.8 $\mu\text{g}/\text{m}^3$ without filtration)  ↓diastolic & systolic BP; ↓CRH & ACTH ↓insulin resistance; ↓8-OHdG, MDA, SOD, 8-iso-PGF2 $\alpha$ , ↓sCD40L, CRP, IL-1 $\beta$ ↔ TNF- $\alpha$ , ICAM-1	Study demonstrated short-term reductions in blood pressure and biomarkers of oxidative stress and inflammation following indoor air purification
Chuang et al 2017	Double-blind, crossover randomized to true/sham filtration  AC electret filter  Living/dining room, master bedroom & guest bedroom  2 x 1 year; no washout	PM <sub>2.5</sub> , VOCs  BP, inflammation (hs-CRP, fibrinogen), oxidative stress (8-OHdG)  Taipai, Taiwan 200 healthy, non-smoking adults; mean age 43 years	PM <sub>2.5</sub> : 43% (12.5 $\mu\text{g}/\text{m}^3$ with filtration & 22.0 $\mu\text{g}/\text{m}^3$ without filtration) VOCs: 67% (0.41 ppm with filtration & 1.25 ppm without filtration).  ↓SBP (6.7%), ↓DBP (6.2%), ↓8-OHdG (53%), ↔fibrinogen, hs-CRP	Long-term indoor air filtration is associated with cardiovascular health of adults
Day et al 2017	Single pass central AHU with coarse filter (F8; MERV 12)-ESP-HEPA filtration split into: • Group A: HEPA & ESP removed from AHU • Group B: ESP removed from AHU	PM <sub>2.5</sub> , O <sub>3</sub>  Respiratory oxidative stress (EBC MDA) Respiratory inflammation (FeNO, EBC pH, nitrate and nitrite) Lung function (FEV1, FVC, FEV1/FVC) Systemic inflammation and oxidative stress (CRP, 8-	Group A: Removal of HEPA & ESP: ↑ PM <sub>2.5</sub> by 38 $\mu\text{g}/\text{m}^3$ ↔ biomarkers  Group B: removal of ESP: ↓O <sub>3</sub> exposure by 2.2 ppb ↓ sCD62P (16.1%) and ↓ SBP (3%)	Results suggest limited physiological responses to PM reductions associated with HEPA filtration, and that ESP use may increase cardiovascular health risk through increasing blood pressure & thrombosis markers

	Office & living quarters 39 days	OHdG, MDA), Vascular tone (SBP, DBP, PP) Arterial stiffness (PWV) Myocardial oxygen supply relative to demand (SEVR) Platelet activation (sCD62P) Endothelial dysfunction (vWF)  Changsha City, China 89 adults working and residing on a working campus; mean age 32 years • Group A: n= 36 • Group B: n= 53		
Shao et al 2017	Double-blind, crossover randomized to true/sham filtration  Portable HEPA  Living room and bedroom  2x 14 d periods; no washout  Participants indoors for 95% of the intervention	PM <sub>2.5</sub> , BC, water soluble organics, NO <sub>3</sub> <sup>-</sup> , SO <sub>4</sub> <sup>2-</sup> , Zn <sup>2+</sup> , Pb <sup>2+</sup> , K <sup>+</sup>  Lung function, inflammation (EBC, fibrinogen, CRP, IL-6, IL-8), HRV, BP  Beijing, China 35 non-smoking adults • with COPD n=20, mean age 67 years • without COPD n = 15, mean age 65.9 years	PM <sub>2.5</sub> : 60% (24 µg/m <sup>3</sup> with filtration & 60 µg/m <sup>3</sup> without); BC: 53% (1.81 µg/m <sup>3</sup> with filtration & 3.87 µg/m <sup>3</sup> without filtration); water soluble organics, NO <sub>3</sub> <sup>-</sup> , SO <sub>4</sub> <sup>2-</sup> , Zn <sup>2+</sup> , Pb <sup>2+</sup> , K <sup>+</sup> : 42-63%  ↓IL-8 (58.59% in the total group & 70.04% in COPD subset); ↔ EBC, fibrinogen, CRP, IL-6, lung function, BP, HRV	Indoor air filtration produced clear improvement on indoor air quality, but no demonstrable changes in the cardio-respiratory outcomes in the seniors living with real-world air pollution exposures.
Cui et al 2018	Double-blind, crossover randomized to true/sham filtration  Portable HEPA  College dormitory  2x 13 h; 14 d washout	PM <sub>2.5</sub> , UFP  Lung function (FEV1, FVC), respiratory inflammation (FeNO), CV function (BP, augmentation index, subendocardial viability rate, heart rate pulse wave velocity); systemic inflammation (IL-6), coagulation (VWF, sCD62P) & oxidative stress (MDA & TBA)  Shanghai, China 70 healthy, non-smoking college students; mean 22 years	PM <sub>2.5</sub> : 72% (10.0 µg/m <sup>3</sup> with filtration & 33.2 µg/m <sup>3</sup> without filtration); UFP: 59%  ↓ Airway impedance (7.1%); ↓ airway resistance (7.4%); ↓ small airway resistance (20.3%); ↓ resonant frequency (4.8%); ↓ VWF (26.9%) ↔ FEV1 & FVC, FeNO, CV function, IL-6, sCD62P, MDA,	A single overnight residential air filtration, capable of substantially reducing indoor particle concentrations, can lead to improved airway mechanics and reduced thrombosis risk.
Zhan et al 2018	6 homes air purifier operated with filter and without filter  Portable HEPA filter  Bedroom	PM <sub>2.5</sub> , organic carbon, elemental carbon, sulfate, nitrate, ammonium, 21 selected metals, PM <sub>2.5</sub> ROS  Personal exposure to PM <sub>2.5</sub> , PM <sub>2.5</sub> components and ROS  Beijing, China	<i>Indoor</i> PM <sub>2.5</sub> : 83% (8.47 µg/m <sup>3</sup> with filtration & 49.0 µg/m <sup>3</sup> without); 70-95% PM <sub>2.5</sub> components; PM <sub>2.5</sub> ROS: clear decrease  <i>Personal exposure</i> Marginal reductions in PM <sub>2.5</sub> (mean: 67.8	Air cleaner can reduce indoor PM <sub>2.5</sub> , all of its major components concentration but was not effective in reducing average 48-hour personal exposure to PM <sub>2.5</sub> .

	48 h	6 participants	and 51.1 µg/m <sup>3</sup> during filtration and control periods respectively) & PM <sub>2.5</sub> components; PM <sub>2.5</sub> ROS: little change	
Barn et al 2018	Randomized to no or 1-2 air purifiers  Portable HEPA filter  Living room for apartments < 40m <sup>2</sup> Living room & bedroom for apartments ≥ 40m <sup>2</sup>  5 mo  No imposed time-activity patterns	PM <sub>2.5</sub> & tobacco smoke  Blood cadmium  Ulaanbaatar, Mongolia 512 Pregnant women (≤18 wks) aged ≥18 years • Intervention group n = 259 • Control group n= 253	PM <sub>2.5</sub> : 29% (17.3 µg/m <sup>3</sup> with filtration & 24.5 µg/m <sup>3</sup> without filtration) PM <sub>2.5</sub> 40% when first applied & 15% after 5 months use  ↓Blood cadmium (14%)	Portable HEPA filter air cleaners can lower indoor PM <sub>2.5</sub> concentrations and SHS exposures in highly polluted settings.

↔; no statistically significant change; ↓ or ↑ statistically different change

8-iso-PGF<sub>2</sub>α: 8-iso-Prostaglandin F<sub>2</sub>α; 8-OHdG: 8-hydroxy-2-deoxyguanosine; AC: air conditioning; ACE: angiotensin-converting enzyme; ACTH: adrenocorticotrophic hormone; BP: blood pressure; COPD: chronic obstructive pulmonary disease; CRH: corticotropin-releasing hormone; CRP: C-reactive protein; DBP: diastolic blood pressure; EBC: exhaled breath condensate; ESP: electrostatic precipitator; ET-1: endothelin-1; FeNO: fractional exhaled nitric oxide; FEV<sub>1</sub>: forced expiratory volume in 1 second; FVC: forced vital capacity; HEPA: high efficiency particle arresting; HRV: heart rate variability; hs-CRP: high sensitivity C-reactive protein; ICAM-1: intracellular adhesion molecule-1; IL-1β: interleukin-1β; IL-6: interleukin-6; IL-8: interleukin-8; MERV: minimum efficiency reporting value; MDA: malondialdehyde; MPO: myeloperoxidase; O<sub>3</sub>: ozone; PAI-1: plasminogen activator inhibitor-1; PM<sub>2.5</sub>: particulate matter < 2.5 µm in diameter; PP: pulse pressure; PWV: pulse wave velocity; sCD40L: soluble CD40 ligand; SBP: systolic blood pressure; SEVR: subendocardial viability ratio; SOD: superoxide dismutase; TNF-α: tumor necrosis factor alpha; t-PA: tissue plasminogen activator; UFP: ultrafine particle; VOC: volatile organic carbon; vWF: von Willebrand factor; WBC: white blood cell count

#### 5.4 Homes afflicted by exceptionally high household air pollution

Nearly 3 million people worldwide are exposed to a complex mixture of inorganic particles and irritant gases as a consequence of burning biomass fuels (wood, charcoal, crop residues and animal dung) on inefficient stoves in poorly ventilated homes, for cooking, lighting, and heating<sup>130</sup>. Although the greatest proportions of exposed populations are in low-income countries of sub-Saharan Africa, India, China and Central America, a significant number of households in high-income countries still rely on solid fuel for heating homes. The magnitude of exposure, when one takes into account exposure intensity, time spent indoors, and the number of individuals exposed, results in a far greater contribution of household air pollution (HAP) to global PM exposure than any other source<sup>131</sup>. Whilst mean 24-h PM<sub>10</sub> levels between 200 and 2,000 µg/m<sup>3</sup> are quite common, peak exposures of > 30,000 µg/m<sup>3</sup> during periods of cooking have been reported<sup>132</sup>. Such emissions are a major contributor to respiratory infections, impaired lung growth, COPD, lung cancer, cataracts and low birth weight<sup>133-135</sup>. Limited evidence also supports associations with CV disease<sup>136</sup>. Initiatives to aggressively reduce HAP exposure focus on a package of interventions that include fuel switching, improving cook stove efficiency, venting emissions and changes in behavior/home layout<sup>137,138</sup>. Some, but not all, studies suggest that certain initiatives may be associated with reduced respiratory symptoms and lung function decline in women and severe pneumonia in children<sup>139-141</sup>. Other trials investigating improved stoves have demonstrated significant improvements in blood pressure<sup>142,143</sup>, ST-segment depression<sup>144</sup> and inflammatory biomarkers<sup>145</sup>. The impact of improved ventilation strategies on HAP have also been investigated<sup>146,147</sup>. Barnes et al<sup>146</sup> used a quasi-experimental design to evaluate a community counseling intervention in rural villages in the North West Province of South Africa on concentrations of PM<sub>10</sub> and CO measured on children younger than five. Whilst

counseling (to encourage burning outdoors when possible, opening at least two sources of ventilation during peak emission times and reducing the amounts of time that children spend in the indoor burning rooms while fires are burning) improved average  $PM_{10}$  and CO concentrations at the personal and micro-environment, post-intervention levels were generally still far above WHO guidelines. Weaver et al<sup>147</sup> tested behavioural and structural ventilation interventions on indoor  $PM_{2.5}$  in Dhaka, Bangladesh in 59 good ventilation (window or door in  $\geq 3$  walls) and 29 poor ventilation (no window, one door) homes. The presence and opening of door(s)/window(s) were inversely associated with the number of hours  $PM_{2.5}$  concentrations exceeded 100 and 250  $\mu g/m^3$ . However owing to several cited barriers to increasing ventilation (outdoor odours/noise, theft risk, mosquito entry, perceptions of wasting electricity) and areas of high ambient  $PM_{2.5}$  concentrations, indoor concentrations were deemed likely to remain above recommended levels. There are as yet no published studies on the use of PAC in homes of developing countries. Of relevance however, McNamara et al<sup>96</sup> compared the efficacy of high versus lower efficiency fiberglass filters in reducing indoor  $PM_{2.5}$ , coarse PM and endotoxin associated coarse PM concentrations in homes in Montana, Alaska and Idaho that use a wood stove for primary heating. Whilst the high efficiency filter showed a 66% reduction in indoor  $PM_{2.5}$  concentrations relative to the lower efficiency model, both interventions significantly reduced coarse PM (63.3% and 40.6% reduction for high and lower efficiency filters respectively) and airborne endotoxin (91.8% and 80.4% reductions respectively), both of which are known respiratory irritants. Whilst these results support the use of high efficiency air filtration units for removing fine particles, the lower efficiency and hence lower cost filter alternatives can be effective for reducing coarse PM and airborne endotoxin in homes burning biomass fuel.

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575 **6.0 Indoor air quality in schools**

576 Schools are a vital element in our societies where children spend up to 5 to 8 hours a day  
577 between the ages of 5 to 18<sup>148</sup>. It is essential therefore that they provide the best possible  
578 infrastructure, not only in terms of teaching but also with respect to climatic conditions  
579 within the learning environment. Unfortunately it is well documented that the IAQ of  
580 schools is invariably unacceptable and since many schools are centrally located within a  
581 community, they are often situated close to major roads and frequent hours coinciding  
582 with high traffic intensities. As a consequence, ambient air in the direct vicinity of school  
583 buildings is often a considerable source of particularly toxic air pollution<sup>149,150</sup>. Within  
584 the classroom exists a multitude of furnishings, educational equipment/materials and  
585 personal items, accommodating large numbers of people engaged in wide-ranging  
586 activities. These unique characteristics give rise to a wealth of emissions from a multitude  
587 of sources<sup>151,152</sup>. Furthermore, whilst regular classroom and hallway cleaning is  
588 important to maintain hygienic environments, intense cleaning procedures can themselves  
589 increase exposure to indoor pollutants<sup>153</sup>. Apart from the presence of airborne emissions  
590 of indoor and outdoor origin, ventilation rates in many schools have been reduced to save  
591 energy. At the same time, owing to inadequate funding, ventilation systems are often  
592 inadequately operated and maintained. Children are also a population group that is  
593 particularly vulnerable to potential health hazards related air pollution exposure owing to  
594 immature and developing organ systems, increased ventilation of the lungs<sup>154,155</sup> and a  
595 compromised ability to deal with toxic compounds<sup>156</sup>. In the classroom it is understood  
596 that poor IAQ could have a negative impact on children's learning. It is therefore of  
597 critical importance to minimize the concentration of air pollution in classrooms,  
598 especially at schools located in close proximity to roadways, to ensure healthy



environments that maximize comfort and enable children to thrive physically and mentally.

### *5.1 Interventions to improve health and learning outcomes in schools through improved air quality*

Several studies have reported associations between inadequate classroom ventilation and children's health and learning outcomes. In a review, Sundell et al<sup>157</sup> concluded that low ventilation rates in schools are associated with increased absenteeism and more respiratory symptoms in children. Since then Mendell et al<sup>158</sup> found that higher classroom ventilation rates were consistently and significantly associated with decreased illness-related absence. Assuming the associations were causal, a cost benefit analysis concluded that keeping ventilation rates below recommended levels in classrooms saves energy and money but has much larger costs from increased health problems and illness among students. Several studies provide strong evidence for making causal associations between school ventilation rates and test performance by children<sup>159-163</sup>. Using crossover experimental designs, Wargocki and Wyon<sup>159,160</sup> showed that increasing the outdoor air delivery rate to Danish classrooms from 5.2 to 9.6 l/s or 3.0 to 8.5 l/s per person significantly improved test speed (but not error rate) performance in approximately 50% of tests. The average CO<sub>2</sub> level (taken as an indicator of human bio-effluents) was reduced from 1300 ppm to 900 ppm and as such the observed effects were assumed to be a consequence of improved classroom air quality. A similar experimental design employed by Bakó-Biró et al<sup>161</sup> in English schools reported significantly improved speed and accuracy in cognitive performance tests upon increasing ventilation rate from 1.0 to 8.0 l/s per person. Effects of suboptimal classroom ventilation on school learning or achievement over time have also been suggested by 2 prospective studies focusing on long-term academic performance<sup>164,165</sup>.

Data on the effectiveness of classroom based air cleaner interventions is very limited (Table 4). Su et al<sup>166</sup> evaluated the performance of upper room ultraviolet germicidal irradiation (UVGI) to reduce bioaerosol concentrations and student absenteeism. Culturable samples – only a fraction of course of all airborne organisms - collected within 10 minutes of students evacuating the UVGI rooms exhibited significantly lower fine (1-8  $\mu\text{m}$ ) but not coarse ( $>8\mu\text{m}$ ) airborne bacteria (but not fungi). This did not translate into reduced overall student absenteeism rates and non-attendance due specifically airborne infectious diseases was not recorded. It should be noted that doors were frequently opened during the measurements, allowing potential infiltration effects from the corridor and beyond. Rosen and Richardson<sup>167</sup> placed electrostatic cleaning systems into two Swedish day care centres (n=63 and n=30 children) during year 2 of a 3-year study and reported reductions in the number of very fine particles of outdoor origin and fine particles produced indoors of 78% and 45% respectively. Absenteeism over the 3-year period due to illness was significantly reduced by 55% in the larger of the two institutions to levels equivalent to those documented in family-based care. Considerable reductions in the concentration of airborne particles were reported in classrooms equipped with electrostatic air cleaners installed mechanically ventilated systems and this effect was greater in rooms with lower outdoor air supply rates<sup>168</sup>. This was not however accompanied by improved performance of a wide range of tasks by children aged 10 to 12 years, children's perception of the classroom environment, symptom intensity or on air quality as perceived by a sensory panel. A pilot randomized controlled trial has also assessed the feasibility of HEPA air cleaners to reduce particulate pollutants in classrooms of asthmatic children in inner-city elementary schools<sup>169</sup>. Sustained (over one year) reductions in classroom  $\text{PM}_{2.5}$  and BC levels were accompanied by a modest improvement in peak flow, but not in forced expiratory volume in 1 second and asthma

649 symptoms. This rather limited effect on asthma morbidity may be related to the fact that  
650 children spend more time outdoors during the warmer months, reducing the efficacy of  
651 improving IAQ.

652

**Table 4. Summary of studies investigating effects of classroom based air cleaner interventions on health and performance**

Study	Study design, purifier type, filtration site, intervention duration	Exposure focus, outcome measures, location, study population	Indoor pollutant reduction & health/performance outcome	Author conclusion
Su et al 2016	UVGI group: n=2 classrooms with 4 upper room UVGI units installed on 4 walls Control group: n=6 classrooms, no units  9 months	Bioaerosol  Student absenteeism  Midwest USA 18-27 students per classroom; third & fourth grade	Reduced fine (1-8 µm) airborne bacteria only when microorganisms were > 160 CFU/m <sup>3</sup> otherwise no effect No effect on coarse (>8 µm) airborne bacteria, airborne fungi  ↔ absenteeism rates	Upper room UVGI can reduce culturable bioaerosols in a crowded environment like classrooms
Rosen & Richardson 1999	Electrostatic air cleaners; 2 day care centres  Installed close to each ceiling-mounted forced air inlet in rooms used by children  Year 2 of a 3-year study	Very fine particles (PM <sub>0.3-3.0</sub> ); fine particles (PM <sub>3-7</sub> )  Non-attendance rates due to illness  Uddevalla, Sweden Day centre A: n=63 children; day centre B: n=30 children; aged 1-6 years	PM <sub>0.3-3.0</sub> : 78%; PM <sub>3-7</sub> : 43%  ↓ 55% illness absenteeism over 3 years in day care centre A	The electrostatic air cleaning technology is cost-efficient and might be a way forward to improve IAQ.
Wargocki et al 2008	Blind crossover; 2 or 3 electrostatic cleaners operating or disabled within 5 pairs of mechanically ventilated classrooms across 5 schools  Wall mounted; one week	Airborne particles  Schoolwork performance, perceived environment, symptom intensity  Denmark N=190 children; aged 10-12 years	↓PNC  ↔ Schoolwork performance, perceived environment, symptom intensity	Although electrostatic air cleaners efficiently reduced the concentration of airborne particles in classrooms, this reduction did not show any of the expected short-term benefits for symptom intensity, environmental perceptions, or the performance of schoolwork for pupils aged 10-12 years
Jhun et al 2017	18 classrooms randomized to 4 air purifiers with (n=9 classrooms) or without (n=9 classrooms) filters  HEPA; classroom floor  1 year	PM <sub>2.5</sub> , BC  PEF, FEV <sub>1</sub> , asthma symptoms  North eastern USA 25 asthmatic children (control n=13; intervention n=12); aged 6-10 years	PM <sub>2.5</sub> : 49% (6.2 µg/m <sup>3</sup> to 2.4 µg/m <sup>3</sup> ) at first follow-up & 42% (6.2 µg/m <sup>3</sup> to 2.6 µg/m <sup>3</sup> ) at second follow-up BC: 58% (0.41 µg/m <sup>3</sup> to 0.13 µg/m <sup>3</sup> ) at first follow-up & 55% (0.41 µg/m <sup>3</sup> to 0.15 µg/m <sup>3</sup> ) at second follow-up  ↔ PEF, FEV <sub>1</sub> , asthma symptoms	A classroom-based air cleaner intervention led to significant reductions in PM <sub>2.5</sub> and BC. Future large-scale studies should comprehensively evaluate the effect of school-based environmental interventions on pediatric asthma morbidity.

↔; no statistically significant change; ↓ or ↑ statistically different change

CFU: colony forming units; BC: black carbon, FEV<sub>1</sub>: forced expiratory volume in 1 second; HEPA: high efficiency particle arresting; PEF: peak expiratory flow; PM<sub>2.5</sub>: particulate matter < 2.5 µm in diameter; UVGI: ultraviolet germicidal irradiation

## 6.0 Air quality in offices

Many urban workers spend approximately 8 hours a day in offices, engaged with a number of people in various activities and often housed within buildings with sealed exterior shells equipped with highly automated HVAC systems. Studies evaluating the air quality in offices have identified electronic equipment, including computers, multifunctional office machines, air conditioners, and particularly photocopiers and printers, as being important sources of PM<sub>2.5</sub>, PM<sub>10</sub>, O<sub>3</sub> and VOCs<sup>170-172</sup>. Poorly ventilated offices also tend to suffer from increased CO<sub>2</sub> as the working day progresses. Good air quality within the office environment is not only be beneficial to personal health (it has been said that around half of the illness affecting the workforce is related to conditions in the work environment), but also has a positive effect on the productivity of the staff.

### 6.1 Interventions to improve IAQ, health and productivity in offices

There is a very large literature base on the effects of office ventilation on productivity and health, which has been widely addressed in several reviews<sup>157,173-175</sup>. A series of well-controlled experimental exposure studies in Denmark, Sweden and the UK have demonstrated that removing common indoor sources of air pollution (floor-coverings, personal computers, used supply air filters) has a significant and positive influence on the productivity of office workers<sup>176-178</sup>. The short-term (up to 5 hours) effects were repeatedly demonstrated even at pollutant levels having no measurable effects on the occupants' perception of air quality. These experimental findings were then validated in field intervention studies conducted in call centers in northern Europe<sup>179</sup> and the Tropics<sup>180,181</sup> where significant positive effects of increased ventilation on productivity (be as high as 6–9%) were recorded. Of note, that the positive findings in the Danish field study were only recorded in the presence of new particulate filters and no filters were

employed in the studies conducted in the Tropics, suggest that used particulate filters in the HVAC system can represent a significant source of pollution. Milton<sup>182</sup> demonstrated that among 3720 employees (and particularly among 600 office workers) of a large US manufacturer, doubling ventilation rates (from 12 to 24 l/s/person) reduced short-term sick leave by 35%. Increased ventilation rates (up to 25 l/s/person) in offices are also associated with reduced SBS symptoms in that drops from 10 to 5 l/s-person increases symptom prevalence by approximately 23% and increases from 10 to 25 l/s-person decreases prevalence by approximately 29%<sup>157,173</sup>. Published studies investigating the efficacy of air cleaning interventions to improve both IAQ of offices and the health of employees is limited to installation of free-standing electrostatic air cleaners as an effective means of breathing zone particle filtration. This approach appears to significantly reduce dust concentration but has no effect on office worker reported symptoms<sup>194-196</sup>.

Modeling efforts focused on filtration systems have found that the overall benefits of use in office buildings are several times larger than the associated running costs<sup>185</sup>. Montgomery et al<sup>186</sup> developed theoretical models of the financial costs and benefits of HVAC air filtration systems in an office in cities around the world representing wide variations in outdoor air quality, electricity prices. Analyses showed that, although the operation cost of filtration systems varied by a factor of 3 between cities, the monetized health benefits of filter installations outweighed the operation costs by up to a factor of 10, and in the majority of scenarios, the net benefits were greatest for the highest efficiency filters. More recent studies have evaluated alternative, energy saving ventilation strategies such as those with dynamic control sequences in modeling the interplay between energy use, profitable IAQ impacts and negative IAQ health impacts due to indoor particle and ozone exposure<sup>187</sup>. Modeling has also suggested that

implementing a high efficiency filter can mitigate negative effects of ventilation whilst higher ventilation rates can increase the efficacy of filtration<sup>188</sup>. The effects of ventilation rate and air filtration efficiency on the chronic health risks associated with indoor VOCs and PM<sub>2.5</sub> concentrations from occupant exposures in offices, schools, grocery, and other retail stores have also been explored using simulation models<sup>189</sup>. Using disability adjusted life years to account for both cancer and non-cancer effects, results indicate that increasing ventilation rates alone is ineffective at reducing chronic disease burdens in these commercial buildings and that alternative strategies such as pollutant source control and the use of particle filtration, should receive greater priority.

## **7.0 Air quality in cars**

Automobiles have become a necessity in modern life to the extent that a significant percentage of the population spends a proportion of time in passenger cars on a daily basis. The microenvironment of vehicle interiors is unique with respect to its relatively small volume and diverse mix of potentially high concentrations of internally generated air pollution<sup>198</sup>, as well UFP emissions from mobile sources (mainly on-road vehicles) that infiltrate the cabin from outside<sup>199</sup>. Pollutants of in-cabin origin include tobacco smoke, biological aerosols and emissions from the wide variety of internal materials (especially in newly produced vehicles) including hard and soft plastics, adhesives, paints and lubricants. Ambient emissions will be particularly high when driving and idling on over congested routes and canyon-like street configurations that hinder dispersive actions and trap pollutants at vehicle level<sup>200</sup>. A significant and disproportionate share of total daily personal exposure to PM can occur within a vehicle cabin, even during short (~30 minute) journeys<sup>201,202</sup>, and systematic reviews conclude that commuters using motorized transport have a higher level of air pollution exposure compared to cyclists and pedestrians<sup>203,204</sup>. Exposure to UFPs in transport microenvironments varies considerably

depending on a number of factors<sup>205</sup>. For instance in-vehicle UFP concentrations result from influx and removal rates and these in turn will be influenced by the rate of air turnover, physical characteristics of the vehicle, driving conditions, in-cabin filter efficiency and particle size<sup>206-208</sup>. Considerable evidence exists from observational and controlled studies linking traffic-related pollution and adverse health effects<sup>209</sup>. Moreover, experimental studies suggest that a biological response to components or a mix of traffic related pollutants can occur following very short-term exposures<sup>210,211</sup>. In-vehicle panel studies provide additional evidence that traffic PM exposures at commonly experienced concentrations among car commuters can be associated with a cardiorespiratory response<sup>212-216</sup>.

#### *7.1 Health benefits of in-cabin air quality interventions (Table 5)*

In a randomized, controlled, cross-over study, Laumbach et al<sup>217</sup> reported decreased oxidative stress in the respiratory tract but no effect on HRV in healthy young participants who rode for 1.5 hours in passenger vehicles during rush-hour traffic wearing air purifying respirators blinded to HEPA filtration. The study was small and the young student population is unlikely to reflect more susceptible populations. The use of cabin air particle filters with active charcoal in an experimental human exhaust study demonstrated significantly reduced symptoms in healthy subjects but no effects on nasal airway lavage, acoustic rhinometry and lung function<sup>218</sup>. Subsequent work by the same group evaluating the efficacy of more developed cabin air filters reported decreased exhaust-induced subjective symptoms but no significant changes in lung function or inflammatory markers<sup>219</sup>. The feasibility of mitigating cardiovascular risks associated with the inhalation of traffic related pollutants by filtering particulate matter from the vehicle passenger cabins has also been investigated<sup>220,221</sup>. During 2-hour exposures to



Southern Californian freeway air, a high-efficiency filtration system within a modified passenger van reduced particle count by 95% but did not remove gases<sup>220</sup>. Whilst most of the vascular and cardiac health endpoints remained unchanged, filtration did result in average decreases in atrial ectopic beat incidence, N-terminal pro B-type natriuretic peptide and vascular endothelial growth factor, suggesting a possible protective effect on atrial arrhythmia. Another study exploring the impact of in-car AC system on air quality improvement and CV health observed decreased HRV indices associated with increased levels of in-car PM<sub>2.5</sub> when the AC was turned off<sup>221</sup>. Turning on the system, using either outside or recirculated inside air, lowered in-car PM<sub>2.5</sub> levels and improved HRV indices. Apart from traffic-related pollutants, another in-cabin health risk stems from exposure, within a confined and often shared space, of airborne infectious agents<sup>222</sup>, allergens<sup>223</sup> and endotoxins<sup>224</sup>. Use of AC systems in the cabin has been shown to effectively reduce by more than 80% of the total number of microorganisms, including bacterial and fungal spores and bioaerosol<sup>225-227</sup>. However, those bacteria and fungi filtered from the air stream by AC filters can proliferate and furthermore, the air stream passing through the vehicle filtration system can aerosolize filter-borne bacteria and fungi reintroducing them back into the vehicle cabin. Indeed, Li et al<sup>228</sup> collected samples of dust from AC and engine filters from 30 cars in 4 four locations of China and studied them for bacteria, fungi, and endotoxins. Dust from their AC filters contained relatively high levels of bacteria (~26,150 CFU/mg), fungi (~1,287 CFU/mg), and endotoxins (~5,527 endotoxin units/mg) including more than 400 different types of bacterial species that included opportunistic pathogens and an abundance of 18 types of allergenic fungal species. The observation of fluorescent peaks around 2.5 µm within the first 5 minutes of AC use was attributed to the aerosolization of filter-borne microbes. To address the question as to whether commercial in-car microbial air decontamination devices can mitigate this risk,

784 Sattar et al<sup>229</sup> tested 3 HEPA filter devices that could be plugged into the car's power  
785 supply. Each device was tested against *Staphylococcus aureus* at their highest fan speeds  
786 in a 3.25 m<sup>3</sup> modified passenger cabin of a 4-door sedan accommodated within a  
787 biosafety level 3 containment facility. The 3 devices took 1.5, 2.3 and 9.7 hours to meet  
788 an arbitrarily set performance criterion constituting the number of hours taken for a 3-  
789 log<sub>10</sub> reduction in the level of airborne challenge bacterium.

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791 **Table 5. Summary of studies investigating health effects of in-car air cleaning interventions**

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Study	Study design, purifier type, intervention duration	Exposure focus, health outcomes, location, study population	Indoor pollutant reduction & health outcome	Author conclusion
Laumbach et al 2014	Single blinded randomized, cross-over: air purifying respirator with or without HEPA filtration  2x 1.5-hr rides in a passenger vehicle in morning rush-hour traffic	No exposure measurement  HRV, oxidative stress (EBC nitrite, sum of nitrite and nitrate, MDA, 8-isoprostane)  New Jersey, USA 21 healthy adults; mean age 22.4 years	-  ↓ 19% EBC nitrite, ↓48% EBC sum of nitrite & nitrate  ↔ malondialdehyde 8-isoprostane, HRV	Increases in markers of oxidative stress in EBC may represent early biological responses to widespread exposures to traffic related air pollution particles that affect passengers in vehicles on heavily trafficked roadways.
Rudell et al 1999	Six one hour chamber exposures to 300 µg/m <sup>3</sup> DDE: 1: air, 2: unfiltered DDE, 3-6: DDE filtered with four different cabin air filters*  *particle filters +/- active charcoal filters	DEP  Subjective symptoms, NAL, acoustic rhinometry, , lung function  Umeå, Sweden 32 healthy adults; age 21-53 years	Particle filters: ↓DEP ↔ symptom intensity, NAL, rhinometry, lung function  Combined particle & activated charcoal filters: ↓DEP ↓symptoms & discomfort ↔ NAL, rhinometry, lung function	The use of active charcoal filters and a particle filter clearly reduced the intensity of symptoms induced by diesel exhaust. Complementary studies on vehicle cabin air filters may result in further diminishing the biomedical effects of diesel exhaust in subjects exposed in traffic & workplaces.
Muala et al 2014	Randomized double-blind controlled crossover to 4 one hour chamber exposures to DE: 1: air; 2: unfiltered DE; 3: DE filtered through particle filter; 4: DE filtered through particle filter with active charcoal	PM <sub>10</sub> , NO <sub>2</sub> , hydrocarbons  Subjective symptoms, lung function (FEV <sub>1</sub> , FVC), inflammation (IL-6, TNFα, P-selectin, sICAM-1, CD40L)  Umeå, Sweden 30 healthy adults; age 21-53 years	Particle filter ↓46% PM <sub>10</sub>  Particle filter plus active charcoal component ↓78% PM <sub>10</sub> ; ↓75% NO <sub>2</sub> ; ↓50% hydrocarbons  ↓symptoms & discomfort ↔ lung function, inflammation	Data demonstrate the effectiveness of cabin filters to protect subjects travelling in vehicles from diesel exhaust emissions.
Hinds et al 2010	Two 2-hour exposures to freeway air* in a 9-passenger van modified with a high-efficiency filtration system delivering (1) filtered or (2) unfiltered air to an exposure chamber inside the van.  *two freeways: one with mostly gasoline vehicles; one with a high proportion of heavy-duty diesel trucks	UFP, PM <sub>2.5</sub> , PM <sub>10</sub> , carbon monoxide, carbon dioxide, BC, PB PAH, oxides of nitrogen  ECG, BP, lung function, inflammation (fibrinogen, IL-6, CRP, MPO, MCP-1); vascular response/injury (sE-selectin, VEGF, sVCAM, sICAM, MMP9, MPO, t-PAI-1), myocardial response to hemodynamic changes (NT-proBNP).  Southern California, USA 19 adults; mean age 71 years	PNC: 95%; PM <sub>2.5</sub> : 81%; PM <sub>10</sub> : 75% BC & PB PAH: 95% Gases: no change  ↓20% atrial ectopic beat incidence ↓30% blood NT pro-BNP & VEGF  ↔ BP, lung function, inflammatory & vascular biomarkers	Study documents a cardiac and vascular response associated with freeway travel that provides new insight into the association of inhalation of traffic related pollutants to arrhythmia...a risk that could be mitigated by filtering particulate matter from the vehicle passenger cabins.
Chuang et al 2013	2 h commute by a car with AC during the morning rush hour AC operation modes:	PM <sub>2.5</sub>  HRV indices (SDNN, r-MSSD)	PM <sub>2.5</sub> in off-mode (35.5 µg/m <sup>3</sup> ), OA-mode (13.2 µg/m <sup>3</sup> ), & IA-mode (16.3 µg/m <sup>3</sup> ),	In-car PM <sub>2.5</sub> is associated with autonomic alteration. Utilization of the car's AC system can improve air quality and modify the

	Use of outside air (OA-mode) Circulating inside air (IA-mode) Off (Off-mode)	Taipei, Taiwan 60 healthy adults aged 20-50 years	Off-mode: 2.7% & 4.1% decreases in SDNN & r-MSSD per IQR increase in in-car PM <sub>2.5</sub>  OA and IA modes: slight decreases in SDNN (OA mode: 0.1%; IA mode: 1.3%) and r-MSSD (OA mode: 1.1%; IA mode: 1.8%) per IQR increase in in-car PM <sub>2.5</sub>	effects of in-car PM <sub>2.5</sub> on HRV indices among human subjects during the commute.
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↔; no statistically significant change; ↓ or ↑ statistically different change

BC: black carbon; CD40L: cluster of differentiation 40 ligand; CRP: C-reactive protein; EBC: exhaled breath condensate; ECG: electrocardiogram; DDE: diluted diesel exhaust; DEP: diesel exhaust particles; FEV<sub>1</sub>: forced expiry volume in 1 second; FVC: forced vital capacity; HEPA: high efficiency particle arresting; HRV: heart rate variability; IL-6: interleukin-6; MDA: malondialdehyde; MMP9: matrix-metalloproteinase-9; MPO: myeloperoxidase NAL: nasal airway lavage; NT pro-BNP: N-terminal pro B-type natriuretic peptide; PB PAH: particle bound polycyclic aromatic hydrocarbons; PM<sub>2.5</sub>: particulate matter < 2.5 µm in diameter; PM<sub>10</sub>: particulate matter < 10 µm in diameter; r-MSSD: square root of the mean of the sum of the squares of differences between adjacent NN intervals; SDNN: standard deviation of NN intervals; sICAM-1: soluble intercellular adhesion molecule-1; sVCAM: soluble vascular cell adhesion molecule; TNFα: tumor necrosis factor-alpha; UFP: ultrafine particle; VEGF: vascular endothelial growth factor

## 8.0 Discussion

Increasing urbanization, technological development and specialized occupational activities have culminated in an 'indoor generation', where most human activities take place within an enclosed space, characterized by a chemically diverse and complex air quality. Source control is, and will always be, the universally preferred approach to reduce contaminants within an indoor setting. This however is becoming increasingly insufficient, technically unfeasible or economically unviable. The second strategy of ensuring sufficient ventilation using air of appropriate quality is also being challenged – by both invariably poor outdoor air quality and our quest for a low carbon economy. Whilst the former directly adds to the burden of indoor air pollution, both factors attract mitigation measures that are leading to efforts to seal off indoor spaces. Depending upon the actions implemented, these measures have the potential of improving or degrading IAQ and as a consequence, health. For instance, dynamic and predictive developments such as demand-controlled and hybrid ventilation, in association with harnessing renewable resources, promise to be effective and efficient strategies. Nevertheless, any repercussions that result in inadequate ventilation will, as research summarized in this review continues to confirm, increase exposure to endogenous indoor air pollutants, heighten health risks (asthma, airway obstruction and SBS symptoms) and curtail concentration, learning and productivity. Further challenges to 'indoor living' relate to the incomplete understanding of the causal associations between indoor air pollutants (aside from CO, formaldehyde, radon and ETS) and health outcomes and unlike ambient air, the relative absence of IAQ measurements, controls/guidance and indices.

Despite the emergence of a wide array of air cleaning technologies, investigations into the effectiveness of personal units in the domestic setting is generally limited to media filtration, largely owing to the lack of investigations on other types of cleaning devices.

Studies have reported that air cleaners equipped with either HEPA filters or electrostatic plates are effective at reducing indoor PM<sub>2.5</sub> concentrations by approximately 30-80% with the majority of this variability attributed to study design (use of one or more units), duration of the intervention, internal air flow and user compliance. With respect to health effects, some of the null associations observed in studies conducted in areas of unremarkable ambient air quality and in wood-smoke communities could in part be explained by small sample sizes, large variations in filtration efficiency, baseline differences in health outcomes and use of medication. In addition, the relatively low baseline pollution concentrations ( $\sim 6.5\text{--}8\text{ }\mu\text{g}/\text{m}^3$ ) and small ( $\sim 3\text{--}4\text{ }\mu\text{g}/\text{m}^3$ ) absolute reductions in indoor PM<sub>2.5</sub> levels following filtration may have limited the ability to detect any relationship between the interventions and health outcomes. The latter however does not resonate with evidence suggesting no threshold exists below which PM<sub>2.5</sub> no longer poses a health risk to the population and thus, the compelling argument for implementing strategies to reduce particulate pollution at both ends of the severity spectrum. Nevertheless, it is interesting that the more notable observations of improved health outcomes stem from studies (generally featuring larger sample sizes and more frequent washout periods) conducted in homes situated in Asian megacities with high baseline indoor air pollution concentrations ( $\sim 22\text{--}96\text{ }\mu\text{g}/\text{m}^3$ ) that underwent substantial absolute reductions ( $\sim 23\text{--}55\text{ }\mu\text{g}/\text{m}^3$  in 5 studies conducted in Beijing or Shanghai;  $9.5\text{ }\mu\text{g}/\text{m}^3$  in one conducted in Taipei) following filtration. Fairly consistent health benefits constituted reductions in BP as well as markers of inflammation, oxidative stress and pro-coagulation pathways following periods ranging from a single overnight filtration to a yearlong intervention<sup>117-120</sup>. Of note, was the one study focusing on an older group of residents, some of whom were COPD patients, that reported no demonstrable changes in a suite of cardio-respiratory outcome parameters<sup>121</sup>, suggesting short term intervention can be of

limited health benefit with exposure to extreme high outdoor air pollution levels. In that indoor air filtration produces clear reductions in indoor pollution concentrations, longer term interventions should be investigated particularly in vulnerable populations (individuals with chronic CV or respiratory disease, children, fetuses, and the elderly) that spend most of their time indoors and as such, could benefit from the clean indoor environment that air purifiers provide. Findings that an air cleaner reduces  $PM_{2.5}$  concentrations within a home but not personal exposure to  $PM_{2.5}$ <sup>128</sup> suggests that study participant activities whilst outdoors without respiratory protection will outweigh the protective effects provided by air filtration within a bedroom and/or living room. Future studies should employ real-time sensors to collect data from all such (indoor and outdoor) activities to quantitatively assess complete exposure profiles as well as housing information such as room area, ventilation rate and an infiltration factor. Furthermore, despite the 54-83% reductions in indoor particulate concentrations achieved by the filtration devices within the urban Chinese homes, average  $PM_{2.5}$  remained high (10 – 24  $\mu g/m^3$ ) probably owing to high outdoor-to-indoor penetration in such highly polluted environments. To this end, calls have been made for large randomized clinical studies among at-risk populations with hard CV endpoints (e.g. prevention of myocardial infarction) to test whether indoor air purifiers with HEPA filters plus outdoor personal-protection (e.g. N95 respirator) result in more substantial reductions in exposure and actual clinical benefits<sup>230</sup>. Such initiatives may provide a mechanism to confirm, or otherwise, the optimistic modelled projected health benefits and costs associated with particle filtration. In schools, numerous investigations have reported the positive effects of increased ventilation and as such, improved IAQ on respiratory symptoms, absenteeism, test performance and long-term academic performance in school children. The proven effectiveness of air filtration systems that are built into school HVAC systems<sup>231,232</sup> as well

as stand-alone air filtration systems in classrooms relying on natural ventilation<sup>233</sup> in reducing indoor pollutants of outdoor origin suggests they represent a critical mitigation measure at schools located near heavily trafficked roads, industry and other important sources of air toxics. Future research should focus on identifying the optimal technologies for removing specific indoor air pollutants (e.g. VOCs versus PM), quantifying short- and long-term health and learning impacts of installing such devices and evaluating the cost benefits resulting from improved IAQ and from a reduction in student exposure to outdoor-infiltrated particles and organic pollutants.

Offices represent another indoor space dedicated to working in which there is a large evidence base indicating that removing common indoor sources of air pollution and increasing ventilation is associated with increased productivity, reduced short-term sick leave, SBS symptoms, inflammation, respiratory infections, asthma and allergy. However whilst such data have attained some consensus within the indoor air research community, a survey by Hamilton et al<sup>234</sup> found that such benefits are not established in the perceptions of US building stakeholders (tenants, owners, operators, and designers/consultants). The minority of respondents thought a ventilation-filtration upgrade would positively impact productivity, absenteeism, or health whilst the majority overestimated costs. Moreover, green building professionals did not represent a group more likely to recognize IAQ benefits, and were less likely to be willing to pay for ventilation and filtration upgrades. These views suggest that to encourage a greater understanding of, and investment in, IAQ-related upgrades in the workplace, requires greater stakeholder education and outreach strategies and possibly, the inclusion of additional building technology to sense and report risks related to IAQ.

Any benefit air cleaning technologies have on human health ultimately relies upon their performance and in the main, this is based upon short-term laboratory tests using tobacco



smoke, aerosolized dust, pollen and potassium chloride particles. Looking forward, to better characterize long-term performance in the real world, necessitates testing against hazardous ultrafine particles that dominate particulate concentrations in outdoor air, over long durations in well-characterized indoor environments to examine primary (beneficial) and secondary (detrimental) impacts<sup>235,236</sup>. Such tests should consider cleaning impacts on multiple contaminants, easily identify common comparative benchmarks such as CADR, single-pass removal efficiency and energy consumption and serve as a clear educational tool regarding optimal usage and maintenance (eg filter changes). As other types of cleaning technologies progress to commercialization, we can look forward to well-designed intervention studies to aid in the selection of particular air cleaners for specific applications. For example confirmation of the potential reliability and durability of PCO technologies that boast low energy consumption credentials is dependent upon developments that can demonstrate (a) high adsorption performance of various VOCs, (b) low/no generation of by-products and catalyst deactivation and (c) an ability of trapping photons from UV to sunlight spectrum<sup>41</sup>. Studies are also focusing on the feasibility of overcoming technology shortcomings by designing hybrid devices from various synergistic combinations of air cleaning techniques<sup>237-239</sup>.

In summary, large-scale international/national interventions as well as personal prevention approaches have the potential to improve the quality of indoor air – an environment where the majority of society spends most of their lives. Between the extremes of this spectrum, the private and the public sector must also address the challenge through the design, construction and maintenance of housing, schools, the workplace and vehicles. Whilst there remains an ongoing role for the three basic strategies (source control, ventilation, air cleaning) to attain this goal, as exposure to indoor environments increases, further emphasis will be placed upon air cleaning technologies. We can undoubtedly look forward

to further research and development of such technologies to drive this field forward from a scientific to a health policy standpoint and in doing ensure that indoor living has a positive impact on health and promotes learning and productivity at work.

## **9.0 Acknowledgement**

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940 **List of abbreviations**

941

942	AC	Air conditioning
943	BC	Black carbon
944	BP	Blood pressure
945	CADR	Clean air delivery rate
946	CO	Carbon monoxide
947	CO <sub>2</sub>	Carbon dioxide
948	COPD	Chronic obstructive pulmonary disease
949	CRP	C-reactive protein
950	CV	Cardiovascular
951	EPA	Environmental Protection Agency
952	ESP	Electrostatic precipitator
953	ETS	Environmental tobacco smoke
954	HEPA	High efficiency particle arresting
955	HVAC	Heating ventilation and air conditioning
956	IL-6	Interleukin-6
957	IAQ	Indoor air quality
958	MERV	Minimum efficiency reporting value
959	MVF	Microvascular function
960	NO <sub>2</sub>	Nitrogen dioxide
961	NO <sub>x</sub>	Oxides of nitrogen
962	O <sub>3</sub>	Ozone
963	PAC	Personal air cleaner
964	PAH	Polycyclic aromatic hydrocarbon
965	PCO	Photocatalytic oxidation
966	PM	Particulate matter
967	PM <sub>2.5</sub>	PM less than 2.5 µm in diameter
968	PM <sub>10</sub>	PM less than 10 µm in diameter
969	SBS	Sick building syndrome
970	SHS	Second hand smoke
971	UFP	Ultrafine particle
972	UVGI	Ultraviolet germicidal irradiation
973	VOC	Volatile organic carbon
974	WHO	World Health Organization

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**Highlights**

- HEPA filter or electret air purifiers reduce indoor PM<sub>2.5</sub> concentrations by 30-80%.
- More consistent health improvements stem from studies in Asian megacity homes.
- Studies should now evaluate longer interventions in vulnerable people with real-time sensors.
- Modelling work reports significant health/performance/economic benefits of air filtration.